REMARKS

Claims 17-19 and 23 are currently pending in this application. Claims 19-22 and 24-31 have been canceled. Claims 17, 18 and 23 have been amended. Support for the language "purified" can be found on page 3, lines 20-22, *et seq.* No new matter has been added. In view of these amendments and of the following remarks, Applicants believe that all the asserted rejections are in condition for withdrawal and all the claims are in condition for allowance.

Claims 17-19 and 23-24 stand rejected under 35 U.S.C. 101 as assertedly being directed to non-statutory subject matter. The Examiner asserts that the claims read on a product that exists in nature, but suggest that the rejection may be obviated by amending the claims to recite an "isolated or purified" chemotaxis-inhibiting protein. Accordingly, Applicants have amended claims 17, 18 and 23 to recite "a purified chemotaxis-inhibiting protein of *Staphylococcus* (CHIPS protein)."

Claims 19 and 23-24 stand rejected under 35 U.S.C. 112, first paragraph, for purported lack of enablement. The Examiner asserts that, while being enabling for a chemotaxis-inhibiting protein from *Staphylococcus aureus*, the specification does not reasonably provide enablement for a medicine or therapeutic composition comprising the chemotaxis-inhibiting protein from *Staphylococcus aureus*. Accordingly, Applicants have canceled claims 19 and 24 and have amended claim 23 to delete the term "therapeutic," thus claim 23 is now directed to "a composition."

Claims 17-19, 23 and 24 stand rejected under 35 U.S.C. 112, second paragraph, for purported indefiniteness. In response to the Examiner's assertions, Applicants have amended claims 17, 18 and 23 to now recite "a purified chemotaxis-inhibiting protein of *Staphylococcus* (CHIPS protein)," have deleted the phrase "which consists of the capacity," and have deleted the phrase "as described in example 1, under 1.2." Claim 17 also has been amended to delete the phrase "and biologically active fragments thereof."

Claims 17-19 and 23-24 stand rejected under 35 U.S.C. 102(b) for purported anticipation by Veldkamp et al. The Examiner asserts that Veldkamp et al. "disclose a soluble mediated protein (SaS) produced by staphylococci that specifically inhibits neutrophil chemotaxis," and "that the SaS specifically down-regulated the expression of the neutrophil fMLP receptor and C5a receptor." The Examiner further asserts that the N-terminal sequence

and the molecular weight of the chemotaxis inhibiting protein would be inherent in the teachings of the prior art. Finally, the Examiner asserts that Veldkamp et al. named this protein CHIPS.

The present invention inheres in a protein, purified from the extracellular medium of growing *Staphylococcus aureus*, having a molecular weight of 17 dK, that has been found capable of blocking, i.e., inhibiting, different granulocytic chemokine receptors specific for chemotactic agents, such as fMLP and C5a. Additionally, this protein has been shown to block the expression of CXCR4 and CCR5 receptors on lymphocytes, monocytes and macrophages.

In contrast to the above, Veldkamp et al. disclose soluble extracellular products from *Staphylococcus aureus* contained in a Staphylococcal culture supernate, referred to as "SaS." (Applicants point out that it is the supernatant that is referred to as "SaS" by Veldkamp et al. and not a soluble mediated protein, as stated by the Examiner). Veldkamp et al. further disclose that this Staphylococcal culture supernate (SaS) down-regulates the expression of the neutrophil fMLP-receptor and the C5a-receptor, while having no effect on IL-8 and PAF receptors. Thus, the relevant disclosure by Veldkamp et al. is that a Staphylococcal culture supernate (SaS) contains something therein, which they refer to as CHIPS, which is capable of down-regulating the fMLP and C5a receptors, thus reducing the ability of neutrophils to migrate towards fMLP or C5a.

Receptor downregulation is the decrease in the amount of receptors expressed on a cell, which can occur in various ways, the binding of a substance thereon being only one way. Thus, Veldkamp et al. does not teach that SaS contains something that is actually blocking the fMLP and C5a receptors. Moreover, Veldkamp et al. would lead one skilled in the art to believe that the SaS is a complex composition containing many constituents, such as toxins, superantigens, and remnants of dead bacteria, such as peptidoglycan, lipoteichoic acid, capsule polysaccharides, glycocalix and cell wall proteins, because culturing bacteria, such as *Staphylococcus aureus*, in a medium generally results in supernatants containing the above-described constituents. Indeed, it is well known in the art that cell wall components, which are not proteins, have an inhibiting effect on chemotaxis, both in bacteria, such as *Staphylococcus aureus*, and in fungi. A person skilled in the art, therefore, first would be directed towards non-protein constituents of the Veldkamp et al. SaS when looking for substances that downregulate the expression of fMLP and C5a receptors.

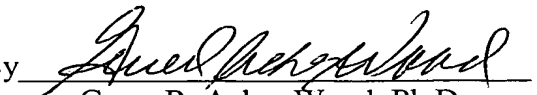
Furthermore, one skilled in the art would not expect that only one constituent of the SaS is responsible for fMLP and C5a receptor downregulation. Receptors for fMLP and C5a exhibit only about 35% homology, and the IL-8 and PAF receptors are about 30% homologous, with the ligands for all these receptors having no structural relationship to one another. (For example, fMLP is a tripeptide, whereas C5a consists of 72 amino acids.) However, Veldkamp et al. disclose that SaS has no downregulatory effect on IL-8 and PAF receptors. It is not, therefore, scientifically plausible that two related receptors with unrelated ligands would be influenced by only one compound, whereas two other related receptors with unrelated ligands would not. Indeed, one would be directed to more than one compound as it is well known in the art that upregulation of receptor expression usually requires more than one factor.

Applicants submit, therefore, that Veldkamp et al. does not teach nor suggest the specific 17 dK chemotaxis-inhibiting protein of the present invention, and indeed one skilled in the art would not look for or expect to find only one factor capable of inhibiting two receptors specific for unrelated ligands that are responsible for the chemotactic movement of neutrophils towards a bacterial target.

For all the foregoing reasons, claims 17, 18 and 23 are patentable over the cited prior art and in condition for allowance. Reconsideration of the rejections and allowance of pending claims 17, 18 and 23 are respectfully requested.

Respectfully submitted,

WEBB ZIESENHEIM LOGSDON
ORKIN & HANSON, P.C.

By 

Gwen R. Acker Wood, Ph.D.
Registration No. 51,027
Attorney for Applicants
700 Koppers Building
436 Seventh Avenue
Pittsburgh, PA 15219-1818
Telephone: 412-471-8815
Facsimile: 412-471-4094
E-mail: webblaw@webblaw.com